International Journal of Infectious Diseases 15 (2011) e201–e205

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Implications of hepatitis C viremia vs. antibody alone on transmission among male injecting drug users in three Afghan cities☆

Abdul Nasir [a], Catherine S. Todd [b,*], Mohammad R. Stanekzai [a], Christian T. Bautista [c], Boulos A. Botros [d], Paul T. Scott [c], Jerome H. Kim [c], Steffanie A. Strathdee [e], Jeffrey Tjaden [d]

[a] International Rescue Committee, Kabul, Afghanistan
[b] Department of Obstetrics & Gynecology, Columbia University, 622W. 168th Street, New York, NY 10032, USA
[c] US Military HIV Research Program, Rockville, Maryland, USA
[d] Virology Research Program, United States Naval Medical Research Unit 3, Cairo, Egypt
[e] Division of International Health and Cross-Cultural Medicine, University of California, San Diego, La Jolla, California, USA

ARTICLE INFO

Article history:
Received 24 June 2010
Received in revised form 9 September 2010
Accepted 5 November 2010

Corresponding Editor: Mark Holodniy, California, USA

Keywords:
Afghanistan
Injecting drug user
HCV
Harm reduction
HIV–HCV co-infection

SUMMARY

Objectives: To assess differences between injecting drug users (IDUs) with hepatitis C virus (HCV) viremia and IDUs with HCV antibody (Ab) or no evidence of prior infection in three Afghan cities.
Methods: IDUs in Hirat, Jalalabad, and Mazar-i-Sharif completed questionnaires and rapid testing for blood-borne infections including HCV Ab. HCV Ab was confirmed with a recombinant immunoblot assay (RIBA); RIBA-positive specimens underwent reverse transcriptase polymerase chain reaction (RT-PCR) for HCV. Risk behaviors associated with viremia were assessed with site-controlled ordinal regression analysis.
Results: Of 609 participants, 223 (36.6%) had confirmed HCV Ab. Of 221 with serum available for PCR evaluation, 127 (57.5%) were viremic. HCV viremia prevalence did not differ by site (range 41.7–59.1%; $p = 0.52$). Among all IDUs, in age and site-controlled ordinal regression analysis, HCV was independently associated with HIV co-infection (adjusted odds ratio (AOR) 7.16, 95% confidence interval (CI) 4.41–11.64), prior addiction treatment (AOR 1.95, 95% CI 1.57–2.42), ever aspirating and re-injecting blood (AOR 1.62, 95% CI 1.18–2.23), prior incarceration (AOR 1.60, 95% CI 1.04–2.45), and sharing injecting equipment in the last 6 months (AOR 1.35, 95% CI 1.02–1.80).
Conclusion: HCV viremia was present in many participants with prior HCV infection and was associated with some injecting risk behaviors, indicating a substantial risk for transmission. Current harm reduction programs should aim to improve HCV awareness and prevention among IDUs in Afghanistan as a matter of urgency.

1. Introduction

Hepatitis C virus (HCV) is a serious health threat for injecting drug users (IDUs), among whom risky practices such as sharing syringes, other injecting equipment, or drug preparations may transmit infection.[1] HCV-associated morbidity among IDUs may manifest as hepatic failure and cirrhosis from chronic infection; this process may be accelerated and amplified by co-infection with HIV or hepatitis B virus (HBV).[1] Acute HCV is symptomatic in 10–15% of cases; those who are asymptomatic in the acute phase of infection are more likely (85–95% vs. 48–75%) to progress to chronic infection.[2]

Injecting drug use is a primary mode of transmission for HCV in developed countries. In developing countries, HCV transmission more commonly results from transfusion and unsafe medical practices.[1,2] However, HCV among IDUs in developing countries has been acknowledged as a burgeoning health issue, particularly in settings where HCV transmission is considered a harbinger of HIV epidemics among this population.[3–5] High HCV prevalence has been recorded among IDUs in many Asian settings, including Pakistan, India, and Iran, several of which are also high HCV burden countries (general population prevalence >2.9%).[1,6–9] The HCV prevalence found among IDUs in two urban settings in Afghanistan has been shown to range from 36.6% to 49.1% and may increase due to the risk of both injection-related and other potential exposures.[10,11] Increasing numbers of IDUs in Afghanistan and the common practice of sharing needles, syringes, injecting equipment

☆ Presented in part as a poster entitled "Prevalence of HIV, viral hepatitis, syphilis and risk behaviors among injection drug users in Hirat, Afghanistan" (MOPE-0280), at the International AIDS Conference, Mexico City, Mexico, August 5, 2008.

* Corresponding author. Tel.: +1 212 305 4805; fax: +1 212 305 6438.
E-mail address: cst2121@columbia.edu (C.S. Todd).

1201-9712/$36.00 – see front matter
doi:10.1016/j.ijid.2010.11.006

and aspirating and re-injecting one's blood ('khoon bozee', literally 'playing with blood') may also contribute to an increasing prevalence of HCV among Afghan IDUs.[10,12]

Longitudinal studies have indicated that some IDUs previously infected with HCV are able to clear subsequent infections; this association persisted after adjustment for risky behaviors.[13,14] However, the risky behaviors that increase the likelihood of re-infection also increase the likelihood of HCV transmission to other IDUs due to the presence of viremia in re-infected individuals. IDUs with measurable viremia may differ significantly with respect to risky behaviors from those with either evidence of past infection or no evidence of prior infection, and are of special interest due to their ability to transmit infection to others. IDUs with viremia may also differ by biological factors; however, it is important to assess the relative association of behavioral factors, as these may be addressed through prevention programs. Our previous cross-sectional study in Kabul was conducted prior to the availability of nucleic acid testing in Afghanistan, so no information could be obtained regarding prevalence and traits associated with viremia. The data presented in this manuscript result from the follow-on assessment conducted between 2006 and 2008 in three other Afghan urban centers.

Recent data from a longitudinal study among IDUs in Kabul revealed high HCV incidence in a setting with many new injectors.[15] Assessment of whether IDUs with detectable viremia are distinct from those with antibody alone may provide important information to prevention programs in other Afghan cities to avert the HCV epidemic currently underway in Kabul. The purpose of this analysis was to determine whether the sub-group of IDUs with HCV viremia differs significantly from IDUs with either no evidence of prior infection or HCV antibody (HCV Ab), and to determine whether behaviors associated with HCV infection are more likely among IDUs with HCV viremia in three Afghan cities.

2. Methods

2.1. Setting

This study was conducted among IDUs in Hirat, Mazar-i-Sharif, and Jalalabad, the largest cities in their respective regions of Afghanistan. At the time of this study, private and public detoxification programs were operating in all cities; there was one harm reduction program operating in the city of Hirat with on-site needle exchange. The other two cities did not have functioning needle and syringe programs (NSPs) and no city had programs offering either opioid substitution therapy or the hepatitis B vaccine to IDUs at the time of the study.

2.2. Study design and participants

This cross-sectional study enrolled participants between September 2006 and January 2008 through the Ministry of Public Health-affiliated Voluntary Counseling and Testing centers (VCT), public and private harm reduction outreach programs (a few of which had VCT services on offer within their organizations), and the International Rescue Committee (IRC) offices in each location. Eligible participants were those reporting injecting drugs (confirmed through physical evidence of recent injection) within the past 6 months, aged 18 years or older, and who were able to provide written informed consent. Participants answered a series of questions to ensure comprehension of the study risks and benefits and the requirements of participation; participants unable to sign their name provided a fingerprint. Approval was obtained from the institutional review boards of the University of California, San Diego, the Walter Reed Army Institute of Research, the US Naval Medical Research Unit 3 in Cairo, Egypt, and the Ministry of Public Health of the Islamic Republic of Afghanistan.

2.3. Measurement of variables and outcomes of interest

The outcomes of interest for this analysis were the determination of whether IDUs with HCV viremia differ significantly from those with prior HCV infection and whether the association between HCV infection and various risky behaviors strengthens in a continuum from seronegative to viremic status. The questionnaire instrument assessed sociodemographic factors, travel, incarceration and medical histories, and drug use and sexual behaviors. Drug use behaviors of interest included sharing needles/syringes ever and in the last 6 months, sharing injecting 'works' (e.g., cookers, cotton) ever and in the last 6 months, duration of injecting, injecting while incarcerated, and aspirating and re-injecting blood. Iatrogenic routes of blood-borne infection transmission were also assessed, such as the receipt of therapeutic injections from both medical and non-medical providers and both the provision and receipt of transfused blood.

2.4. Procedures

Potential participants were recruited by experienced outreach workers affiliated with local harm reduction programs in each city. Trained study staff obtained informed consent, administered the study questionnaire, and performed rapid testing and counseling in a private setting. Laboratory methods for other pathogens have been reported in a related publication.[16] Briefly, whole blood rapid testing for HCV Ab was performed using Standard Diagnostics HCV Ab (Standard Diagnostics, Kyonggi-do, Korea). The manufacturer reports 100% sensitivity and 94.1% specificity by World Health Organization (WHO) evaluation.[17] Serum specimens were obtained from participants with positive rapid tests; HCV Ab was confirmed with a recombinant immunoblot assay (RIBA 3.0 SIA®, Chiron Corp., Emeryville, CA, USA). The presence of HCV was assessed with a qualitative reverse transcriptase polymerase chain reaction (RT-PCR). Extraction was performed using the QiAamp Viral RNA Mini Kit (Qiagen Inc., Germantown, MD, USA) according to the manufacturer's instructions. A nested RT-PCR was performed as previously described, with minor modifications of cycle parameters and master mix components.[18] Both RIBA and PCR were performed at the Afghan Public Health Institute laboratory in Kabul, with the exception of HBV PCR, which was performed at the United States Naval Medical Research Unit 3 (NAMRU-3) laboratory in Cairo, Egypt.

Confirmatory results were available after 2 weeks; participants were provided with follow-up appointments at the time of enrollment. All participants received post-test counseling, risk reduction counseling, a small non-monetary gift of hygiene items (e.g., razor, soap) of US$4 value, condoms, and sterile syringes, with referrals for detoxification programs upon request. No data were recorded on those declining or ineligible for study entry. Enrollment was conducted for 12 months at all sites.

2.5. Statistical analysis

Descriptive statistics for viremic individuals were generated, with site differences assessed using the Chi-square test. Risky behaviors, such as sharing syringes and injecting works, were reported by frequency; these variables were dichotomized into ever/never in the last 6 months.

Univariate logistic regression was performed to identify potential associations between HCV viremia and select demographic, biological, and individual risk behavior variables, controlled by enrollment site, of all confirmed HCV Ab-positive participants. Variables were entered into a site- and age-adjusted multivariable model if they were associated with HCV viremia at

Table 1
Demographic and behavioral characteristics of male injecting drug users with HCV viremia in three Afghan cities ($n = 127$)

Feature	Hirat	Jalalabad	Mazar-i-Sharif	p-Value
HCV viremia; % of HCV Ab-pos IDUs who were viremic/site ($n = 221$)	58.2% (96)	41.7% (5)	59.1% (26)	0.520
Age, years, mean (SD)	30.2 (7.3)	27.2 (6.3)	31.5 (9.1)	0.006
Age initiated injecting, years, mean (SD)	27.3 (7.0)	24.2 (4.3)	26.2 (7.9)	0.736
Civil status: ever married, % (n)	46.9% (45)	80% (4)	42.3% (11)	0.299
Education: ≤6 years, % (n)	35.4% (34)	60% (3)	30.8% (8)	0.457
Lived/worked outside Afghanistan in last decade, % (n)	95.8% (92)	60% (3)	76.9% (20)	<0.001
Ever in jail: Yes, % (n)	76.8% (73)[b]	40% (2)	73.1% (19)	0.177
Injected in jail:[a] Yes, % (n)	16.9% (12)[c]	0 (0)	21.1% (4)	0.767
Shared syringes in last 6 months: Yes, % (n)	26.1% (24)[d]	80% (4)	19.2% (5)	0.018
Shared injecting works last 6 months: Yes, % (n)	38.5% (37)	0 (0)	19.2% (5)	0.049
Aspirating and re-injecting blood: Yes, % (n)	78.1% (75)	80% (4)	92.3% (24)	0.261
Prior addiction treatment: Yes, % (n)	76.0% (73)	40% (2)	26.9% (7)	<0.001

HCV, hepatitis C virus; Ab, antibody; pos, positive; IDU, injecting drug user; SD, standard deviation.
[a] Denominator is number ever having been incarcerated/site.
[b] Of 95 respondents.
[c] Of 71 respondents.
[d] Of 92 respondents.

the 10% level in univariate analysis or were considered of epidemiological significance.

Ordinal logistic regression was performed to identify associations between various HCV infection states and select demographic and risk behavior variables, adjusting for site and age. The reference group was defined as participants with no evidence of prior HCV infection (antibody-negative by rapid test or by RIBA), assigned the value of 0, with confirmed HCV Ab-positive participants assigned the value of 1 and those with HCV Ab and detectable viremia assigned the value of 2. A multivariable model was generated to identify factors independently associated with HCV infection states using the Wald test to determine which variables were retained at $p < 0.05$. The proportional odds assumption of ordinal regression was tested using the Brant test.

3. Results

Of 623 IDUs recruited in the three Afghan cities (Hirat $n = 340$, Jalalabad $n = 96$, and Mazar-i-Sharif $n = 187$), eight female IDUs were excluded as the low number of female participants precluded accurate description and adjustment by sex. As stated in the Methods, only participants with confirmed HCV Ab by RIBA were included in the subsequent analyses. Of 615 total male participants, 609 had HCV rapid testing performed. Of 229 participants with reactive HCV rapid tests with serum available for RIBA, 223 were RIBA-reactive, two were RIBA-indeterminate, and four were negative (positive predictive value 97.4%). Two of the 223 male IDUs with reactive RIBA tests did not have sufficient serum available for PCR testing and were excluded, leaving 221 for the analysis.

The overall prevalence of RIBA-confirmed HCV Ab was 36.6% ($n = 223/609$), with significant variance by site ($p < 0.001$). Of 221 participants with HCV Ab and sufficient available specimen for PCR testing, 127 (57.5%) had detectable viremia. There was no significant difference in prevalence of viremia among IDUs with positive HCV Ab by site, with 41.7% in Jalalabad, 59.1% in Mazar-i-Sharif, and 58.2% in Hirat. However, there were significant site differences among viremic individuals by age, sharing syringes/needles or injecting paraphernalia, having lived outside the country in the last 10 years, and having previous addiction treatment (Table 1). Further, age alone was positively associated with viremia (odds ratio (OR) 1.04, 95% confidence interval (CI) 1.00–1.08). Due to these differences by site and age, all further analyses were controlled for these factors. All detected HIV cases were positive for HCV Ab and were enrolled in Hirat. Reported therapeutic injections in the last 6 months (13.4%, $n = 17$), therapeutic injections by a non-medical provider (3.1%, $n = 4$), and blood donation (7.1%, $n = 9$) or transfusion at any time (4.7%, $n = 6$) were rare among viremic IDUs.

Table 2
Factors independently associated with HCV viremia among HCV antibody-positive injection drug users in three Afghan cities, controlling for site and age ($n = 221$)

Variable	AOR (95% CI)
HIV co-infection	1.47 (1.29–1.66)
HBV co-infection	0.48 (0.43–0.51)
Share syringes in last 6 months	0.40 (0.29–0.55)

HCV, hepatitis C virus; HIV, human immunodeficiency virus; HBV, hepatitis B virus; AOR, adjusted odds ratio; CI, confidence interval.

Table 3
Variables independently associated with HCV viremia among male injecting drug users in three cities of Afghanistan in ordinal logistic regression, controlled for age and site ($N = 609$)

Variable	AOR (95% CI)
HIV co-infection	7.16 (4.41–11.64)
Prior addiction treatment	1.95 (1.57–2.42)
Ever aspirate and re-inject blood	1.62 (1.18–2.23)
Ever been incarcerated	1.60 (1.04–2.45)
Shared injecting equipment last 6 months	1.35 (1.02–1.80)
Ever received injection from non-medical provider	0.30 (0.10–0.89)

HCV, hepatitis C virus; HIV, human immunodeficiency virus; AOR, adjusted odds ratio; CI, confidence interval.

Injecting behaviors and other risk markers were compared between IDUs with HCV viremia and those with HCV Ab only (Table 2). HIV co-infection was positively independently associated with HCV viremia, but HBV co-infection and sharing syringes or needles in the last 6 months were negatively associated in age- and site-controlled multivariable regression.

In age- and site-controlled ordinal logistic regression analysis, the spectrum (range 0–2) of HCV disease from antibody to viremia was independently associated with HIV co-infection, prior incarceration, sharing injecting equipment in the last 6 months, khoon bozee, and prior addiction treatment, while a negative association between HCV infection and ever receiving therapeutic injection from a non-medical provider persisted (Table 3).

4. Discussion

Circulating virus was present in at least 40% of participants with HCV Ab and did not vary significantly by site, ensuring a

substantial risk of HCV transmission within injecting networks inclusive of these IDUs. We acknowledge that this figure likely underestimates viremia, as sustained viremia without detectable antibody levels has been noted among IDUs in longitudinal studies in the Netherlands and the USA.[19–21] Though not statistically significant, IDUs in Jalalabad were less likely to have detectable viremia. One possible reason for this observation may be the social organization of injectors in Jalalabad, where many participants lived outside the city center, had initiated injecting in small networks affiliated with the opium processing industry, and only came to the city for addiction treatment or trade reasons (personal communication, Dr M. Nasiry, assistant study manager, Jalalabad).

In comparisons between viremic IDUs and IDUs with HCV Ab alone, the odds of viremia increased with age. Viremia was less likely for older IDUs on opioid replacement therapy in Australia, suggesting that the observed association in Afghanistan may be behavioral rather than physiological.[22] One hypothesis for this observation may be that injecting networks tend to consist of individuals of similar age, seen as peers. HIV co-infection was positively associated with HCV viremia, similar to findings among IDUs in several urban centers in the USA.[23,24] Grebely et al., in a longitudinal study, found that IDUs with HIV co-infection have higher rates of HCV clearance; however, incident HCV re-infection was twice as high among HIV-infected individuals.[14] The clearance rate among those with HCV re-infection was 29% (4/14); none of the six HIV-infected participants re-infected with HCV cleared their viremia.[14] Sharing needles/syringes in the last 6 months was negatively associated with viremia, which is surprising as this group would likely be at greater risk for recent infection or re-infection, as noted among the Canadian cohort.[14] The negative association between detectable viremia and HBV viremia may be explained by the observed higher HCV clearance rates in the presence of chronic HBV infection, similar to findings among hemophiliac and female patient populations.[25,26]

Several behaviors or conditions were progressively more associated with the presence of both viremia and HCV Ab. The strongest association was between HIV co-infection and HCV, likely reflective of both infections resulting from some of the same risky behaviors, as noted in China, Iran, and India.[6,27,28] Prior incarceration was associated with increasing odds of HCV, potentially reflecting sharing of injecting equipment and mixing of injecting networks in prison settings, previously detected in a variety of settings.[6,29,30] Similarly, previous addiction treatment may reflect mixing of injecting networks during or following the course of treatment, as participants in this study reflect active IDUs who have relapsed.

Sharing injecting 'works' (e.g., cookers, cotton) in the last 6 months was associated with the HCV spectrum but not with HCV viremia among those with HCV infection. This association was unexpected, as recent risk behaviors would seem more likely to be linked to viremia present in recent infection/re-infection.[31,32] We did not assess whether ever sharing works was associated with HCV viremia, as recent behaviors were deemed more relevant. Sharing of needles and syringes and potentially injecting works may be under-reported or may have ceased due to these messages. Participants enrolled in Hirat, most of whom had been refugees in Iran and were exposed to harm reduction messaging in that setting, had a higher prevalence of HCV Ab. Though analyses were controlled for site, under-reporting in Hirat of sharing, a stigmatized behavior, may have influenced results. Aspirating and re-injecting blood was independently associated with chronic HCV infection and may serve as a proxy for risky sharing behaviors, as hypothesized for IDUs in Pakistan.[9]

Receipt of a therapeutic injection from a non-medical provider was positively associated with the presence of HCV antibody among IDUs in Kabul, which was the rationale for including this variable in our analysis.[10] This variable was negatively associated with HCV in our ordinal analysis and, though this relationship was statistically significant, there were relatively few individuals in any group reporting prior injections from non-medical providers. We believe these low numbers indicate a spurious relationship. Of note, reported receipt of a therapeutic injection ever or in the last 6 months was similarly rare. Other potential markers of iatrogenic transmission will be considered in future studies.

Due to cost limitations, we did not obtain serum samples or perform PCR for participants with negative HCV Ab rapid tests. Therefore, we are unable to comment on circulating virus among participants with HCV infection without detectable antibody, such as those with acute (<12 weeks) infection, immune compromise, or delayed/absent humoral response.[2,19] Further, the number of participants with viremia may have been further underestimated based on the threshold for detecting virus with the qualitative PCR assay used. This assay may not have been sensitive enough to detect those participants who were chronically infected but had low circulating viral levels.[19] The rapid tests used cite a sensitivity of 100%, indicating that true positives were unlikely to have been missed in the initial screening.[17] However, though the manufacturer's fact sheet states the evaluation was performed by the WHO, no WHO source could be identified to confirm the findings. The performance characteristics of the rapid test may also have been affected by setting. Additionally, risky injecting practices were based on self-report and may have been under-reported. We did not map injecting networks and so cannot comment on risk behaviors within specific networks as related to HCV prevalence. Last, we did not assess HCV genotype, a factor known to affect both viral load and probability of natural clearance.[33] Future genotype assessment is planned and will provide important information for treatment recommendations.

A high prevalence of HCV viremia has been detected among IDUs previously exposed to HCV in three cities in Afghanistan. This suggests ample opportunity for HCV transmission among IDUs through shared injecting equipment and potentially to the population at large through shared medical equipment. IDUs in Afghanistan are vulnerable to this infection and efforts must be focused on scaling up harm reduction programs to limit further HCV transmission in this population. Currently, harm reduction programs are being established or expanded in Hirat, Jalalabad and Mazar-i-Sharif, indicating the feasibility of harm reduction programs in Afghanistan, despite conservative culture, political instability, and armed conflict. Encouragingly, the Kabul harm reduction programs have established a harm reduction kit that is provided to IDUs in the field and includes sterile saline water bottles, cotton gauze, and alcohol prep pads in addition to unused syringes. We recommend that as voluntary HIV counseling and testing is scaled up with harm reduction efforts, counseling and testing for HCV and sterile injecting paraphernalia also be provided to this vulnerable group to prevent further expansion of this prevalent infection and associated morbidity and mortality.

Acknowledgements

We thank the Ministries of Counter Narcotics and Public Health; the Mazar-i-Sharif, Jalalabad, and Hirat VCT centers; the Action Aid/University of Manitoba study team; the Shahomat Rehabilitation Organization; and the Demand Reduction Action Team programs for their assistance. We thank Ms Kathy Fiekert for her assistance with database management. We dedicate this work to the memory of Dr Boulos Botros. Last, we thank our participants for their time and trust.

This study was funded by the Walter Reed Army Institute of Research. The opinions and assertions made by the authors do not reflect the official position or opinion of the US Department of the

Navy or Army, or of the respective in-country National HIV/AIDS Control Programs and other non-governmental organizations (NGOs). Dr Todd appreciates support from the Fogarty International Center of the National Institutes of Health (K01TW007408). Study sponsors had no involvement in study design, data collection or analysis, or in the writing or decision to submit the manuscript.

Conflict of interest: AN, CST, MRS, CTB, BAB, PTS, JHK, SAS, and JT declare they have no conflict of interest.

Ethical approval: The study protocol was approved by the institutional review boards (IRBs) of University of California, San Diego, US NAMRU-3, Walter Reed Army Institute of Research, and the Afghan Ministry of Public Health prior to study conduct. The research study experienced a 6-month lapse of NAMRU-3 IRB approval; this lapse occurred following completion of participant enrollment.

References

1. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005;**5**:558–67.
2. Maheshwari A, Ray S, Thuluvath PJ. Acute hepatitis C. *Lancet* 2008;**372**:321–32.
3. Azim T, Chowdhury EI, Reza M, Faruque MO, Ahmed G, Khan R, et al. Prevalence of infections, HIV risk behaviors and factors associated with HIV infection among male injecting drug users attending a needle/syringe exchange program in Dhaka, Bangladesh. *Subst Use Misuse* 2008;**43**:2124–44.
4. Kageyama S, Agdamag DM, Alesna ET, Abellanosa-Tac-An IP, Corpuz AC, Telan EF, et al. Tracking the entry routes of hepatitis C virus as a surrogate of HIV in an HIV-low prevalence country, the Philippines. *J Med Virol* 2009;**81**:1157–62.
5. Des Jarlais DC, Arasteh K, Semaan S, Wood E. HIV among injecting drug users: current epidemiology, biologic markers, respondent-driven sampling, and supervised-injection facilities. *Curr Opin HIV AIDS* 2009;**4**:308–13.
6. Zamani S, Ichikawa S, Nassirimanesh B, Vazirian M, Ichikawa K, Gouya MM, et al. Prevalence and correlates of hepatitis C virus infection among injecting drug users in Tehran. *Int J Drug Policy* 2007;**18**:359–63.
7. Platt L, Vickerman P, Columbien M, Hasan S, Lalji N, Mayhew S, et al. Prevalence of HIV, HCV and sexually transmitted infections among injecting drug users in Rawalpindi and Abbottabad, Pakistan: evidence for an emerging injection-related HIV epidemic. *Sex Transm Infect* 2009;**85**(Suppl 2):ii17–22.
8. Mahanta J, Medhi GK, Paranjape RS, Roy N, Kohli A, Akoijam BS, et al., IBBA study team. Injecting and sexual risk behaviours, sexually transmitted infections and HIV prevalence in injecting drug users in three states in India. *AIDS* 2008;**22**(Suppl 5):S59–68.
9. Kuo I, ul-Hasan S, Galai N, Thomas DL, Zafar T, Ahmed MA, et al. High HCV seroprevalence and HIV drug use risk behaviors among injection drug users in Pakistan. *Harm Reduct J* 2006;**3**:26.
10. Todd CS, Abed AM, Strathdee SA, Scott PT, Botros BA, Safi N, et al. HIV, hepatitis C, and hepatitis B infections and associated risk behavior in injection drug users, Kabul, Afghanistan. *Emerg Infect Dis* 2007;**13**:1327–31.
11. Nasir A, Todd CS, Stanekzai MR, Bautista CT, Strathdee SA, Scott PT, et al. Prevalence of HIV, viral hepatitis, syphilis and risk behaviors among injection drug users in Hirat, Afghanistan. Abstract MOPE-0280. *Programs and Abstracts of the 17th International AIDS Conference, Vol. 1 (Mexico City)*. 2008.p. 118.
12. United Nations Office on Drugs and Crime (UNODC). Afghanistan drug use survey 2005. Kabul, Afghanistan: UNODC; 2006.
13. Mehta SH, Cox A, Hoover DR, Wang XH, Mao Q, Ray S, et al. Protection against persistence of hepatitis C. *Lancet* 2002;**359**:1478–83.
14. Grebely J, Conway B, Raffa JD, Lai C, Krajden M, Tyndall MW. Hepatitis C virus reinfection in injection drug users. *Hepatology* 2006;**44**:1139–45.
15. Todd CS, Nasir A, Stanekzai MR, Rasuli MZ, Fiekert K, Orr MG, et al. Hepatitis C and HIV incidence among injecting drug users in Kabul, Afghanistan. Abstract MOPDC101. *XVIII International AIDS Conference*. 2010.
16. Todd CS, Nasir A, Stanekzai MR, Bautista CT, Botros BA, Scott PT, et al. HIV, hepatitis B, and hepatitis C prevalence and associated risk behaviors among female sex workers in three Afghan cities. *AIDS* 2010;**24**(Suppl 2): S69–75.
17. Standard Diagnostics. SD Bioline HCV factsheet. Available at: http://standardia.com/html_e/mn03/mn03_01_00.asp?intId=13 (accessed November 30, 2010).
18. Ray SC, Arthur RR, Carella A, Bukh J, Thomas DL. Genetic epidemiology of hepatitis C virus throughout Egypt. *J Infect Dis* 2000;**182**:698–707.
19. Beld M, Penning M, van Putten M, van den Hoek A, Damen M, Klein MR, et al. Low levels of hepatitis C virus RNA in serum, plasma, and peripheral blood mononuclear cells of injecting drug users during long antibody-undetectable periods before seroconversion. *Blood* 1999;**94**:1183–91.
20. Thomas DL, Vlahov D, Solomon L, Cohn S, Taylor E, Garfein R, et al. Correlates of hepatitis C virus infections among injection drug users. *Medicine (Baltimore)* 1995;**74**:212–20.
21. Hall CS, Charlebois ED, Hahn JA, Moss AR, Bangsberg DR. Hepatitis C virus infection in San Francisco's HIV-infected urban poor. *J Gen Intern Med* 2004;**19**:357–65.
22. Hallinan R, Byrne A, Amin J, Dore GJ. Hepatitis C virus prevalence and outcomes among injecting drug users on opioid replacement therapy. *J Gastroenterol Hepatol* 2005;**20**:1082–6.
23. Fishbein DA, Lo Y, Netski D, Thomas DL, Klein RS. Predictors of hepatitis C virus RNA levels in a prospective cohort study of drug users. *J Acquir Immune Defic Syndr* 2006;**41**:471–6.
24. Thomas DL, Rich JD, Schuman P. Multicenter evaluation of hepatitis C RNA levels among female injection drug users. *J Infect Dis* 2001;**183**:973–6.
25. Operskalski EA, Mack WJ, Strickler HD, French AL, Augenbraun M, Tien PC, et al. Factors associated with hepatitis C viremia in a large cohort of HIV-infected and –uninfected women. *J Clin Virol* 2008;**41**:255–63.
26. Zhang M, Rosenberg PS, Brown DL, Preiss L, Konkle BA, Eyster ME, et al., Second Multicenter Hemophilia Cohort Study. Correlates of spontaneous clearance of hepatitis C virus among people with hemophilia. *Blood* 2006;**107**:892–7.
27. Zhang C, Yang R, Xia X, Qin S, Dai J, Zhang Z, et al. High prevalence of HIV-1 and hepatitis C virus coinfection among injection drug users in the southeastern region of Yunnan, China. *J Acquir Immune Defic Syndr* 2002;**29**:191–6.
28. Solomon SS, Srikrishnan AK, Mehta SH, Vasudevan CK, Murugavel KG, Thamburaj E, et al. High prevalence of HIV, HIV/hepatitis C virus coinfection, and risk behaviors among injection drug users in Chennai, India: a cause for concern. *J Acquir Immune Defic Syndr* 2008;**49**:327–32.
29. Dolan K, Kite B, Black E, Aceijas C, Stimson GV, Reference Group on HIV/AIDS Prevention and Care among Injecting Drug Users in Developing and Transitional Countries. HIV in prison in low-income and middle-income countries. *Lancet Infect Dis* 2007;**7**:32–41.
30. Sarang A, Rhodes T, Platt L, Kirzhanova V, Shelkovnikova O, Volnov V, et al. Drug injecting and syringe use in the HIV risk environment of Russian penitentiary institutions: qualitative study. *Addiction* 2006;**101**:1787–96.
31. Micallef JM, Macdonald V, Jauncey M, Amin J, Rawlinson W, van Beek I, et al. High incidence of hepatitis C virus reinfection within a cohort of injecting drug users. *J Viral Hepat* 2007;**14**:413–8.
32. Aitken CK, Lewis J, Tracy SL, Spelman T, Bowden DS, Bharadwajet M, et al. High incidence of hepatitis C virus reinfection in a cohort of injecting drug users. *Hepatology* 2008;**48**:1746–52.
33. Lehmann M, Meyer MF, Monazahian M, Tillmann HL, Manns MP, Wedemeyer H. High rate of spontaneous clearance of acute hepatitis C virus genotype 3 infection. *J Med Virol* 2004;**73**:387–91.